

5083

CLAIMS for the UNITED STATES

1. An isolated human survival motor neuron (SMN) protein.
2. An isolated mouse survival motor neuron (SMN) protein.
3. A human SMN gene T-BCD541 comprising a cDNA sequence of Figure 3.
4. A human SMN gene according to Claim 3, which comprises the following intronic sequences:

- for intron n° 6 :

5' AATTTTAAATTTTGTAGAGACAGGGTCTCATATGTTGCCAGGGTG  
GTGTCAAGCTCCAGGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGT  
GGGATTGTAGGCATGAGCCACTGCAAGAAACCTTAACTGCAGCCTAATAATT  
GTTTCTTTGGGATAACTTTTAAAGTACATTAAAGACTATCAACTTAATTTT  
TGATCATATTGTGTTGAATAAATAAGTAAATGTCTTGTGAACAAAATGCTT  
TTTAACATCCATATAAAGCTATCTATATATAGCTATCTATGTCTATATAGCTA  
TTTAACTTCCTTTTATTTTCCTTACAG 3'

- for intron n° 7 :

5' GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTTGTAAACTTTAT  
GGTTTGTGGAACAAATGTTTTGAACAGTTAAAAGTTCAGATGTTAAAA  
GTTGAAAGGTTAATGTAACAATCAATATTAAAGAATTTTGATGCCAAACT  
ATTACATAAAAGGTTAATCTACATCCCTACTAGAATTCTCATACTTAACTGGT  
TGGTTATGTGGAAGAAACATACTTTCACAATAAAGAGCTTTAGGATATGATGC  
CATTTTATATCACTAGTAGGCAGACCAGCAGACTTTTTTTTATTGTGATATGG  
GATAACCTAGGCATACTGCACTGTACACTCTGACATATGAAGTGCTCTAGTCA  
AGTTTAACTGGTGTCCACAGAGACATGGTTTAACTGGAATTCGTCAAGCCTC  
TGGTTCTAATTTCTCATTTGCAG 3'

5184

5. The SMN gene according to Claim 3, which hybridizes in stringent conditions with the sequence of Figure 3 used as probe.

6. An isolated variant of the SMN gene, which variant is a C-BCD541 gene comprising a cDNA sequence of Figure 2.

7. An isolated nucleotide sequence comprising nucleotides 34 to 915 of the sequence of Figure 3.

8. An isolated nucleotide sequence comprising nucleotides 34 to 915 of the sequence of Figure 2.

9. An isolated DNA sequence encoding a survival motor neuron (SMN) protein of Figure 1 or Figure 8.

10. An isolated nucleotide sequence, comprising at least around 9 nucleotides within a sequence of <sup>cDNA sequence of Fig. 3</sup> Claim 3 or hybridizing <sup>under stringent</sup> in stringent conditions with a sequence of any one of Claims <sup>2</sup> 1 to 9.

11. A mouse SMN gene comprising a cDNA sequence corresponding to the sequence of Figure 12.

12. A probe comprising the isolated nucleotide sequence of Claim 10.

13. A probe comprising the isolated nucleotide sequence of Claim 11.

14. An isolated nucleotide sequence selected among the following sequences :

5' AGACATCAACTTAATTCTGATCA 3'  
5' TAAGGAATGTGAGCACCTTCTTC 3'  
5' GTAATAACCAATGCAATGTGAA 3'  
5' CTACAACACCCTTCTCACAG 3'

[illegible]

85 52

- 15. A set of primers comprising :**  
 - a pair of primers contained in the sequence comprising nucleotides 921 to 1469 of the sequence of Figure 3 and/or  
 - a pair of primers comprising the following sequences :

5' AGACTATCAACTTAATTTCTGATCA 3'  
5' TAAGGAATGTGAGCACCTTCCTTC 3'

- 16. A set of primers selected from the group consisting of:**

5' ACACTATCAACTTAATTTCTGATCA 3'  
5' TAAGGAATGTGAGCACCTTCCTTC 3';

5' GTAATAACCAATGCAATGTGAA 3'  
5' CTACAACACCCTTCTCACAG 3'

5' AGG GCG AGG CTC TGT CTC A 3'  
5' CGG GAG GAC CGC TTG TAG T 3' ;

5' GCC GGA AGT CGT CAC TCT T 3'  
5' GGG TGC TGA GAG CGC TAA TA 3' ;

5' TGT GTG GAT TAA GAT GAC TC 3'  
5' CAC TTT ATC GTA TGT TAT C 3' ;

5' CTG TGC ACC ACC CTG TAA CAT G 3'  
5' AAG GAC TAA TGA GAC ATC C 3' ;

5' CGA GAT GAT AGT TTG CCC TC 3'  
5' AG CTA CTT CAC AGA TTG GGG AAA G 3' ;

Sub B3

53 86

5' CTC ATC TAG TCT CTG CTG CC 3'  
5' TGG ATA TGG AAA TAG AGA GGG AGC 3' ;

5' CAC CCT TAT AAC AAA AAC CTG C 3'  
5' GAG AAA GGA GTT CCA TGC AGC AG 3' ;

5' GAG AGG TTA AAT GTC CCG AC 3'  
5' GTG AGA ACT CCA GGT CTC CTG G 3' ;

5' TGA GTC TGT TTG ACT TCA GG 3'  
5' GAA GCA AAT GGA GCC AGC CAG C 3' ;

5' TTT CTA CCC ATT AGA ATC TGG 3'  
5' CCC CAC TTA CTA TCA TGC TGG CTG 3' ;

5' CCA GAC TTT ACT TTT TGT TTA CTG 3'  
5' ATA GCC ACT CAT GTA CCA TGA 3' ;

5' AAG AGT AAT TTA AGC CTC AGA CAG 3'  
5' CTC CCA TAT GTC CAG ATT CTC TTG 3' ;

5' AGA CTA TCA ACT TAA TTT CTG ATC A 3'  
5' TAA GGA ATG TGA GCA CCT TCC TTC 3' ;

5' AGA CTA TCA ACT TAA TTT CTG ATC A 3'  
5' GTA AGA TTC ACT TTC ATA ATG CTG 3' ;

5' CTT TAT GGT TTG TGG AAA ACA 3'  
5' GGC ATC ATA TCC TAA ACC TC 3' ;

33-1-42660890

5' CGA GAT GAT AGT' TTG CCC TC 3'  
5' AG CTA CTT CAC AGA TTG GGG AAA G 3'

5' CTC ATC TAG TCT CTG CTT CC 3'  
5' TGG ATA TGG AAA TAG AGA GGG AGC 3'

5' CAC CCT TAT AAC AAA AAC CTG C 3'  
5' GAG AAA GGA GTT CCA TGG AGC AG 3'

5' GAG AGG TTA AAT GTC CCG AC 3'  
5' GTG AGA ACT CCA GGT CTC CTG G 3'

5' TGA GTC TGT TTG ACT TCA GG 3'  
5' GAA GGA/AAT GGA GGC AGC CAG C 3'

5' TTT CTA CCC ATT AGA ATC TGG 3'  
5' CCC CAC TTA CTA TCA TGC TGG CTG 3'

5' CCA GAC TTT ACT TTT TGT TTA CTG 3'  
5' ATA GCC ACT CAT GTA CCA TGA 3'

5' AAG AGT AAT TTA AGC CTC AGA CAG 3'  
5' CTC CCA TAT GTC CAG ATT CTC TTG 3'

5' AGA CTA TCA ACT TAA TTT CTG ATC A 3'  
5' TAA GGA ATG TGA GCA CCT TCC TTC 3'

55<sup>n</sup> 88

5' AGA CTA TCA ACT TAA TTT CTG ATC A 3'  
 5' GTA AGA TTC ACT TTC ATA ATG CTG 3'

5' CTT TAT GGT TTG TGG AAA ACA 3'  
 5' GGC ATC ATA TCC TAA AGC TC 3'

5' GTA ATA ACC AAA TGC AAT GTG AA 3'  
 5' CTA CAA CAC CTT TTT CAG AG 3'

5' GGT GTC CAC AGA GGA CAT GG 3'  
 5' AAG AGT TAA CCC ATT CCA GCT TCC 3'

17. Antisense nucleotide sequence which is an invert complementary sequence of a sequence according to any one of Claims 3 to 9 and 11

18. An isolated human survival motor neuron (SMN) protein comprising the amino acid sequence of Figure 1.

19. A protein according to Claim 18, which is truncated and which comprises the sequence of Figure 8.

20. An isolated mouse survival motor neuron (SMN) protein comprising the amino acid sequence of Figure 12.

21. Kit for the in vitro detection of motor neuron diseases, comprising :  
 - a set of primers according to any one of Claims 15 or 16 ;  
 - reagents for an amplification reaction ; and  
 - a probe for the detection of the amplified product.

22. Kit for the in vitro detection of motor neuron diseases, comprising a probe according to Claim 12.

33-1-42660890

B

Sub G<sub>1</sub>

56 89

B Sub G<sub>2</sub>

23. Kit according to Claim ~~21~~ or 22, for the detection of SMA.

B

24. Cloning or expression vector, characterized in that it comprises a sequence according to any one of Claims ~~1 to 11~~ <sup>Claims 3 to 9 and 11</sup>.

25. Vector according to Claim 24, characterized in that it has a motor neuron tropism.

26. Vector according to Claim 25, characterized in that it is for example a poliovirus, an adenovirus or a herpes virus.

27. Vector according to Claim 24, characterized in that it is a retrovirus vector.

B

28. Host cell, for example bone marrow cells, fibroblasts, epithelial cells, characterized in that it is transformed by a vector according to ~~any one of Claims 24 to 27~~ <sup>Claim 24</sup>.

B

29. Recombinant nucleotide sequence, characterized in that it comprises a sequence of any one of Claims ~~1 to 11~~ <sup>3 to 9 and 11</sup> and a sequence capable of encoding a polypeptide having a tropism for the motor neuron.

30. A method for detecting motor neuron disorders including spinal muscular atrophy, any trophic lateral sclerosis and primary lateral sclerosis, said method comprising the steps of :

- (a) extracting DNA from a patient sample;
- (b) amplifying said DNA with primers according to any one of Claims 15 or 16;
- (c) subjecting said amplified DNA to SCCP;
- (d) autoradiographing the gels; and
- (e) detecting the presence or absence of the motor neuron disorder.

Sub G<sub>3</sub>

add B<sub>4</sub> add G<sub>8</sub> Add I<sub>9</sub>